

**Remarks**

The Applicants address the Examiner's remarks in the order he presented them.

**The Objection Regarding the Specification**

The Examiner objected that the specification lacks descriptive section headings. The Applicants respectfully point out that the MPEP merely suggests, but does not require, such headings. Nonetheless, to advance prosecution of the application, the Applicants have added the headings the Examiner suggested. They respectfully request that he withdraw his objection to the specification.

**The First Rejection Under § 112, First Paragraph**

The Examiner rejected claims 70-80 and 82-92 under 35 U.S.C. § 112, first paragraph. The Applicants have amended claim 82 and respectfully submit that claims 82-90, as amended, fully comport with the requirements of § 112, first paragraph. The Applicants respectfully request that the Examiner withdraw the rejection of claims 82-90 under that section.

Regarding claims 70-80, the Examiner stated that the specification does not enable a module "not being in a reaction system." Office Action, at 4, ln 11. The Applicants respectfully disagree. The specification describes in detail the composition of such a module; Figure 3 illustrates it, and the text accompanying the illustration describes its components. The text at pages 17-18, for example, describes a membrane module comprising two groups of spaces; the text following it, through page 22, describes "a few considerations" relating to permeability coefficients and other characteristics of the module. One of ordinary skill in the art should have no difficulty constructing such a module, especially in view of the detailed description of it the specification provides.

The Examiner's argument appears to be that the specification does not enable the module of the invention because the module is not in a reaction system. But there is no reason why an applicant is not permitted to claim a component of an invention if the component itself is novel and unobvious. The specification teaches how to make and use such a component. The Applicants respectfully submit, therefore, that claims directed to it are proper.

For the foregoing reasons, the Applicants respectfully request that the Examiner withdraw the rejection of claims 70-80 under § 112, first paragraph.

The First Rejection Under § 112, First Paragraph

The Examiner rejected claims 50, 51, 61, and 62 under 35 U.S.C. § 112, second paragraph. The Examiner found the term "plate module" in claim 50 confusing. "Plate module" is a species of membrane module; it is not, as the Examiner suspects, a non-membrane module. The Specification describes a plate module at page 19. It speaks (at lines 26-28) of a "extremely high ratio of membrane area to volume.. ." The Applicants respectfully request that the Examiner withdraw the rejection of claim 50 under § 112, second paragraph.

The Applicants have canceled claim 51.

As to claims 61 and 62, the Examiner objected that the claims do not recite proper Markush language. The Applicants have amended the claims, and respectfully request that the Examiner withdraw the rejection of them under § 112, second paragraph.

The Rejection Under 35 U.S.C. § 103(a)

The Examiner objected to claims 32-92 under 35 U.S.C. § 103(a) as being obvious in view of the Portner and Märkl reference (R. Portner and H. Märkl, Appl. Microbiol. Biotechnol. 50:403-414 (1998)). Figure 3a of the reference discloses a reactor where air is supplied to a culture chamber separated from a dialyzing chamber by a dialyzing membrane, and from this the Examiner argues that "it would have been obvious to supply air to space containing circulating culture liquid containing cells in the dialysis module . . . to prevent cells from suffering oxygen limitation." Office Action, at 7, Ins. 7-13. The Applicants respectfully disagree.

The modification the Examiner has described – supplying air to a dialysis module – is *not* the Applicants' invention. The invention comprises, instead, a reaction system in which one introduces *two gases* to the system; in claim 39, for example, one introduces a first gas into the culture fluid in the space for culturing cells, and a second gas into the culture fluid in the membrane module. The Examiner acknowledges this, stating that Portner and Märkl does not disclose the step of "supplying gas to culture fluid in the dialysis module (membrane module)." Office Action, at 6, Ins. 22-24. Nowhere does the Portner and Märkl reference

suggest that one can introduce two gases into a reaction system. There is only one gas introduced into the system in every reaction system the reference describes.

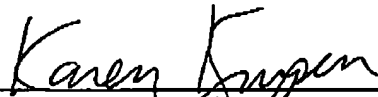
The Portner and Märkl reference (and the Applicants point out that one of them authored that reference) does not address the principal difficulty facing the Applicants at the time they conceived their invention: that scaling up existing production techniques to several m<sup>3</sup> involves several difficulties, owing, in part, to the limited mechanical strength of dialyzing membranes. This is a significant problem, because "the mechanical strain in the culture space is very high, since it is necessary to introduce large amounts of air or oxygen to supply to . . . organisms [while] [a]t the same time, large amounts of carbon dioxide have to be removed." Specification, at ¶ 3. The Examiner does not address this problem. He states that it would have been obvious to add air to the culture liquid "to prevent cells from suffering oxygen limitation as described on page 404." But merely fixing the "oxygen limitation" problem does not address problems of scale. *Nowhere* does the Portner and Märkl reference suggest that by supplying a first gas and a second gas to the same system, one can achieve the large scale capacity of the present system – and, indeed, the Examiner does not even allege that it does so. For this reason, the reference cannot render the Applicants' invention obvious.

The Applicants respectfully submit that the Portner and Märkl reference does not disclose or suggest the present invention. They respectfully request that the Examiner withdraw the rejection under § 103(a).

#### Conclusion

The Applicants respectfully submit that the claims, as amended, are in condition for allowance, and respectfully request early, favorable action on the application. Should the Examiner believe that an interview would advance the prosecution of this application, the Applicants invite him to contact the undersigned at 908.231.4658.

Respectfully submitted,



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